Mindfulness-based cognitive therapy efficacy in reducing physiological response to emotional stimuli in patients with bipolar I disorder and the intermediate role of cognitive reactivity

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Abstract

Bipolar disorder is associated with altered emotional reactivity, and literature suggest that Mindfulness-Based Cognitive Therapy (MBCT) could have beneficial effects on emotion regulation. This study aims to investigate its impact on the physiological component of emotional response by using skin conductance recording, and to investigate a potential mediating or predictive effect of cognitive reactivity.

Sixty-seven patients with bipolar I disorder were assessed at baseline, pre-MBCT and post-MBCT. After answering self-reported inventories regarding depression (BDI-13) and dysfunctional attitudes (DAS), each patient was instructed to focus on 36 emotional pictures (12 negative, 12 positive and 12 neutral) derived from the International Affective Pictures System (IAPS) while electrodermal responses were recorded.

MBCT strongly reduce dysfunctional attitudes and is beneficial in reducing the amplitude of the physiological response to negative stimuli. Findings also show~~s~~ that higher baseline level of dysfunctional attitudes ~~at~~ predict larger reduction of physiological reactivity after MBCT.

MBCT could decrease patient’s reactivity while facing stimuli with negative emotion by decreasing its physiological component, which is coherent with the aim of MCBT to facilitate disengaging from affective stimuli. Further studies are needed to better understand the mechanisms involved in electrophysiological responses, and how this effect could translate in reducing the risk of relapse.

Key words: *MBCT, bipolar disorder, emotions, physiological reactivity, dysfunctional attitudes*

Introduction

Bipolar I disorder is associated with disruptions in emotion regulation. Bipolar patients exhibit abnormal patterns of emotional reactivity (Dargél et al., 2017; Etain et al., 2017; Henry et al., 2014; Gruber et al., 2013; Gruber, 2011; Henry et al., 2010; Henry et al., 2008; Phillips, Ladouceur & Drevets, 2008; Johnson et al., 2007), greater and longer emotional responses to emotional stimuli (Stratta et al., 2014; Gruber et al., 2008; Knowles et al., 2007; Forbes et al., 2007; Farmer et al., 2006) and inappropriate emotions regulation strategies (Gruber et al., 2012; Kim et al., 2012; Miklowitz et al., 2010 ; Johnson et al., 2008).

Mindfulness-Based Cognitive Therapy (MBCT) showed promising results on clinical improvement in bipolar patients (Lovas and Schuman-Olivier, 2018; Weber et al., 2017; Perich et al., 2013; Ives-Deliperi et al., 2013; Deckersbach et al., 2012; Weber et al., 2010; Miklowitz et al., 2009; Williams et al., 2008; Kenny and Williams, 2007). MBCT might indeed help disengaging from affective stimuli by developing self-regulation of attention (Desbordes et al., 2014; Bishop et al., 2004). It has also been shown to facilitate emotion regulation (Cosme and Wiens, 2015; Chambers, Guillone & Allen, 2009; Roemer et al., 2009; Farb et al., 2007; Feldman et al., 2007) and to decrease reactivity to emotional pictures (Taylor et al., 2011; Ortner, Kilner & Zelazo, 2007; Arch & Craske, 2006;). With many convergent findings showing the benefit of MBCT in bipolar disorder, the mechanisms underlying these effects have surprisingly not been clearly identified.

An emotional response can be defined by several components, one of them being the physiological response (Kleinginna and Kleinginna, 1981). The latter can be measured through, for example, the recording of skin conductance. Using emotional pictures, Ortner and colleagues (2007) found that mindfulness can help decrease physiological reactivity, suggesting that the impact of mindfulness on emotion regulation could be understood through its effects on the physiological component of emotions. Moreover, mindfulness mediation has been shown to decrease physiological markers of stress and anxiety (such as cortisol, blood pressure and heart rate) in a range of population (Pascoe & Crewther, 2016; Pascoe et al., 2020). Given the focus of mindfulness in modifying our relationships to body sensations and internal experiences (Cahn and Polish, 2006), it is coherent to expect that MBCT can improve physiological emotional reactivity. Yet, this has been seldom studied among bipolar patients, despite previous literature showing that bipolar disorder is associated with increased physiological correlates of emotional responding (e.g., respiratory sinus arrhythmia, neuroimaging) (Gruber, Harvey & Johnson, 2009; Gruber et al., 2011; Hassel et al., 2008).

Previous studies found a positive effect of MBCT for bipolar patient on negatives mood states and mood regulation (Chadwick et al., 2011), using objective measures (Howells et al., 2014; Ives-Deliperi et al., 2013; Strakowski et al., 2012). But to our knowledge, its impact on physiological reactivity has not been studied using skin conductance.

Moreover, our understanding of the mechanisms involved in MBCT efficacy in improving emotional reactivity still need to be expanded. Several studies suggested that emotion regulation and emotional reactivity might be influenced by cognitive factors. For example, cognitive reappraisal has been shown to be an effective strategy to reduce the emotional impact of a situation (Gross, 2002) and decreased negative emotion (Gross & John, 2003) or neural activity in the amygdala and insula (Ochsner & Gross, 2005). It has also been suggested that MBCT efficacy may be mediated by a reduction of 'cognitive reactivity' (Williams et al., 2000; Kuyken et al., 2010), a concept related to negative beliefs reactivated when negative mood states occur (Segal, 1988). Previous studies (Perich et al., 2013; Kuyken et al., 2010) showed in fact that MBCT reduces scores of dysfunctional attitudes, which can be considered as a marker of cognitive reactivity.

The present study aims to investigate the impact of MBCT on bipolar patients' emotional response by focusing on the physiological component through skin conductance recording. We also aim to explore the mechanisms involved in MBCT efficacy on physiological reactivity, by investigating the meditating and predictive effect of dysfunctional attitudes.

Method

Participants and procedure

Sixty-seven outpatients addressed for MBCT and currently meeting DSM-5 criteria for bipolar I disorder according to the SCID-I (First et al., 2002) were recruited.

Inclusion criteria were: (a) patients euthymic or with subsyndromal symptoms at the beginning of the study (BDI<7; YMRS<6) and not currently meeting criteria for depressive or manic episodes; (b) patient not receiving any psychotherapy; (c) patients currently under pharmacological treatment for bipolar disorder.

Patients were assessed 2 months before MBCT (baseline), immediately before MBCT (pre-treatment) and immediately after MBCT (post-treatment). All participants gave their written informed consent to participate, and the protocol was approved by the Regional Ethic Committee (Clinical Trial NCT02472483). The study was conducted according to ethics recommendations in the Helsinki declaration (World Medical Association, 2013).

MBCT intervention consisted in a standard protocol of 8-week program including 2-hour weekly sessions (Segal, Williams & Teasdale, 2002), and was led by two trained therapists with at least 3 years of experience with MBCT. Therapy sessions included guided mindfulness practices (i.e., body scan, sitting meditation) and teaching of cognitive-behaviorale skills.
Patients were asked to practice mindfulness meditation at least 30 minutes per day to develop moment-to-moment awareness, attentional monitoring and acceptance.

Clinical assessment

The Beck Depression Inventory (BDI-13, Beck et al., 1961) was used to assess depressive symptomatology and the Dysfunctional Attitudes Scale (DAS, Weissman, 1978) for dysfunctional attitudes and beliefs.

Emotional response investigations

Three sets of visual stimuli[1] were selected from the International Affective Picture System (IAPS) (Lang et al., 2008), including 12 positive, 12 negative and 12 neutral pictures (Lemaire et al., 2014).

The autonomic measures were monitored using a 16-channel PowerLab system (AD Instruments, Bella Vista, NSW, Australia) connected to a PC. The bioelectrical signals were filtered and amplified before being fed into the analog input connector of the PowerLab unit.

Skin conductance was recorded with the ML116 GSR Amplifier (AD Instruments) of the 16-Channel PowerLabsystem. The dry electrodes were attached with a Velcro strap on the palmar surfaces of the distal phalange of the second and third fingers of the non-dominant hand.

Measurements were displayed in µSv. Following initial procedure (Clarke et al., 2016), there were two measures of electrodermal response (SCR): 1) the presence of a significant change of the electrodermal response, defined as a change of at least 0.04 µSv in conductance starting in the 1-4s intervals after onset of each visual stimulus, and 2) the amplitude of the response, which was calculated only for patients having a significant change of SCR response. Prior to measurements, electrodermal activity at baseline level was defined by a recording in the presence of a neutral visual stimulus.

[1] Negative: 2683, 2710, 2800, 3180, 3350, 3530, 6212, 6312, 6350, 6510, 9810, 9910; Neutral: 2038, 2102, 2191, 2214, 2393, 2396, 2411, 2514, 2595, 2635, 2880, 2890; Positive: 1441, 2035, 2340, 2347, 4659, 4660, 4668, 4680, 5621, 5825, 5833, 8370.

The IAPS pictures were displayed as a succession of 12 trios, each trio including one negative, one neutral, and one positive picture. Each picture was displayed for 6s. The effect of presentation order was limited by ensuring that negative, neutral, and positive images were revealed in a balanced presentation order (M'bailara et al., 2009).

At baseline, pictures were presented a second time and participants were asked to provide a subjective evaluation in order to determine if the valence (positive, negative, neutral) of each picture was correctly perceive. Participants were asked to rate the valence (degree of pleasantness) and arousal (intensity of emotion) for each picture, using the Self-Assessment Manikin (SAM) (Bradley & Lang, 1994). Participants' responses were recorded using the E-Prime 2.0 software (Psychology Software Tools, Pittsburgh, PA), and each picture was presented twice.

Data analysis

All statistical analyses were conducted using SPSS version 22.0 for Windows (IBM, Armonk, NY, USA). Normal distributions of variables were checked using Kolmogorov-Smirnov Test prior to analysis. χ^2, student t-test and variance analysis followed by post-hoc tests were used to examine differences between baseline, pre-treatment and post-treatment or between pleasant, unpleasant and neutral pictures. Considering that SCR amplitude was included in the analyses only for patients with a change of the SCR response over 0.04 μSv, a Wilcoxon non-parametric test was used (the sample size being lower than 20). Effect size differences were calculated using Cohen's d (Sawilowsky, 2009; Cohen, 1988).

Path analyses were conducted using PROCESS statistics for SPSS, in order to test for the mediating effect of dysfunctional attitudes improvement in the impact of MBCT on physiological reactivity. Linear regression analyses were conducted to investigate the predictive effect of DAS scores at baseline on the reduction of the physiological response.

Results

Sociodemographic and psychological characteristics are presented in *table 1*. DAS scores ($p<0.001$) and BDI scores ($p=0.002$) significantly decreased from pre-treatment to post-treatment, but not from baseline to pre-treatment (waiting list) ($p>0.05$). The subjective emotional evaluation confirmed that positive, negative and neutral pictures were evaluated by patients as such (F=478,211, $p<0.001$), and that perceived arousal was higher for emotional compared to neutral pictures (F=307.604, $p<0.001$) (*table 1*).

Emotional pictures were always associated with a higher percentage of patients having a significant change of the electrodermal response compared to neutral pictures ($\chi^2=7.54$, p=0.023 at baseline, $\chi^2=11.12$, p=0.004 at pre-treatment and $\chi^2=14.62$, p=0.001 at post-treatment). Time did not impact the percentage of patients with a significant change in the electrodermal response: no difference has been found between baseline, pre-treatment and post-treatment for negative ($\chi^2=0.575$, p=0.750), positive ($\chi^2=0.620$, p=0.733) and neutral ($\chi^2=0.078$, p=0.962) pictures.

Both positive and negative pictures were associated with higher SCR amplitude at baseline (Z=-2,711, p=0.007; Z=-2,333, p=0.026) and pre-treatment (Z=-2.281, p=0.023; Z=-1.929, p=.054) compared to neutral pictures, the size effects being 'very high' (*d*=1.496 for positive pictures and *d*=1.544 for negative pictures at baseline, *d*=1.366 for positive pictures and *d*=1.644 for negative pictures at pre-treatment).

At post-treatment, only positive pictures (Z=-2.160, p=0.031, *d*=1.286) remain associated with higher SCR amplitude compared to neutral pictures, but no difference was found regarding negative pictures (Z=-1.658, p=0.097). No difference was found between positive and negative pictures, regardless of time (p=0.466 at baseline, p=0.681 at pre-treatment, p=0.537 at post-treatment).

SCR amplitude decreased from pre-treatment to post-treatment for negative pictures (p=0.042), the size effect being medium (*d*=0.734). Results also suggested that SCR amplitude also decreased from pre-treatment to post-treatment for positive pictures as well (p=0.075), although this was only a trend. No significant difference was found regarding neutral pictures, nor from baseline to pre-treatment when considering all types of pictures (*table 1 and figure 1*).

A path analysis (*figure 2*) showed a direct effect of MBCT on SCR amplitude reduction for negative stimuli (β=0.37, R^2=0.111, t=2.265, p=0.034).

MBCT also had a significant effect on DAS improvement (β=0.384, R^2=0.147, t=4.775, p<0.001), and the path analysis suggested a trend effect of DAS improvement on SCR amplitude reduction for negative stimuli (β=0.327, R^2=0.079, t=1.959, p=0.059).

When DAS improvement was added as a mediator, the effect of MBCT on SCR amplitude reduction for negative stimuli was no longer significant (p=0.183), suggesting a mediating role of DAS improvement, according to Baron and Kenny criteria (1986). However, the bootstrapping indirect effect of MBCT on SCR amplitude reduction for negative stimuli through DAS improvement was not significant (CI 95% [(-0.05)-(0.34)].

When assessing the impact on positive stimuli, neither MBCT (t=0.966, p=0.343) nor DAS improvement (t=0.865, p=0.395) significantly predicted SCR amplitude reduction.

When BDI improvement was tested as an intermediate factor, we observed that MBCT significantly predicted BDI improvement (β=0.339, R^2=0.115, t=4.147, p<0.001), but BDI improvement was not related to SCR amplitude reduction (t=1.601, p=0.119 for negative pictures, t=-0.234, p=0.817 for positive pictures).

Linear regression analysis showed that when controlling for age and sexe, lower DAS scores at baseline were predictive of a higher SCR amplitude reduction for negative pictures ($p=0.039$). No predictive effect of DAS scores was observed on the SCR amplitude reduction for neutral and positive stimuli ($p>.05$) (*table 2*).

Discussion

The main goal of the present study was to assess the effects of MBCT on the physiological component of emotional reactivity in bipolar I using skin conductance recording. Our secondary objective was to examine the role of dysfunctional attitudes on the impact of MBCT on physiological responses.

The main findings indicate a beneficial effect of MBCT on both cognitive (i.e. dysfunctional attitudes) and physiological reactivity, with a decreased SCR amplitude for negative stimuli. This suggests that MBCT could improve emotional reactivity by impacting its physiological component. However, no difference in the percentage of patients having a significant change of SCR was observed. In others words, MBCT may be more efficient to attenuate the peak amplitude of SCR and to reduce recovery time needed after a negative stimulus, rather than to decrease the intensity of the initial physiological response. This hypothesis would be coherent with the fact that mindfulness does not aim to directly modify emotion, but rather to facilitate the disengagement process (Segal & Walsh, 2017**;** van der Velden et al., 2015).

Previous investigations showed improved emotions regulation in bipolar patients receiving MBCT (Howells et al., 2014; Ives-Deliperi et al., 2013; Strakowski et al., 2012; Chadwick et al., 2011). Our findings extend this research to MBCT effect on the physiological response that can be involved in emotion regulation, and help confirming that skin conductance could be a relevant measure to investigate MBCT effect on emotional reactivity.

Considering that both negative and positive pictures were initially associated with stronger electrodermal response, we could have expected that MBCT was also associated with a decreased SCR amplitude for positive stimuli, but that was not the case in our sample. However, SCR amplitude was initially higher for negative stimuli compared to positive stimuli, and SCR amplitude for positive stimuli was also decreased after MBCT, although these differences were not significant. This result stresses the need to replicate the study with a larger sample, results needing to be considered carefully due to the smaller sample size of the SCR amplitude measures.

Furthermore, we can hypothesize that during practice, participants tend to focus their training more on negative emotions rather than positive ones; thus developing better capacities to regulate their attention regarding negative stimuli. We can also imagine that after developing self-regulation of attention with MBCT training, patients tried voluntarily to use those ability on unpleasant sensations; but not on pleasant ones which they are less likely to want to disengage from.

Patients with bipolar disorder display heightened emotional responding to positive stimuli (Gruber, Harvey & Johnson, 2009; Gruber et al., 2011), which help differentiate bipolar disorder from unipolar depressive disorder (Kring & Bacchorowksi, 1999). Considering that our findings suggested that MBCT were not efficient to decrease reactivity to positive stimuli, this could point out the necessity to develop therapeutic strategies focused on the regulation of positive emotions.

Our findings also help to confirm MBCT efficacy on reducing cognitive reactivity (Perich et al., 2013; Kuyken et al., 2010), and suggest that cognitive reactivity could be involved in physiological reactivity. This support the idea that negative and irrational believes existing in bipolar patients can impact emotional reactivity when negative mood states are experienced, and suggest that enhancing cognitive flexibility could help decrease emotional reactivity as well

(Bishop et al., 2004; Segal, 1988). This could also partly explain that physiological reactivity to positive pictures was not as decreased as for negative pictures, considering that it is less likely to be impacted by cognitive reactivity which target the reactivation of negative believes.

Results also lead to the hypothesis that cognitive reactivity and physiological reactivity may share similar mechanisms, and that improving attentional flexibility trough MBCT could help disengaging from both negative thoughts and negative sensations.

These hypothesis are coherent with previous studies showing that dysfunctional attitudes and irrational believes measured by the DAS are positively associated with physiological arousal and negative emotions such as sadness or disgust (Tehranchi, Neshatdoost & Amiri, 2018; Kuiper, Olinger & Martin, 1988); two emotions which are particularly targeted by IAPS negative pictures and are known to be involved in depression (Tehranchi et al., 2018; Power & Tarsia, 2007).

However, the indirect effect of MBCT on SCR amplitude through DAS improvement was not significant, suggesting that both cognitive reactivity reduction and physiological reactivity reduction could be supported by others potential mediators which are yet to be investigated. Once again, the smaller sample used for SCR amplitudes analysis also promotes the need to investigate the potential mediating role of DAS improvement in a larger sample.

Finally, cognitive reactivity at baseline was predictive of the reduction of the physiological response to negative stimuli, which suggest that severe cognitive reactivity before therapy may impact the efficacy of MBCT on emotional regulation. This is coherent with previous literature showing that cognitive reappraisal, which is altered by cognitive reactivity and dysfunctional attitudes, is an efficient strategy for emotional regulation (Gruber, Hay & Gross, 2014). We may thus hypothesize that patients with strong dysfunctional attitudes are less likely to improve their emotional regulation skills during MBCT. Therefore, one could suggest that patients with bipolar disorders that display severe cognitive reactivity may benefit cognitive therapeutic strategy focused on improving cognitive reappraisal prior to MBCT.

Several limitations should be considered in drawing conclusions from the present finding. First, patients were not randomized and were not compared to a control group. This would help ensure that the observed evolution was related to MBCT, and not to non-specific treatment factors such as acclimation to the stimuli. The electrodermal responses might indeed be sensible to habituation, which could impact the observed reduction of the emotional response and should be controlled in further studies On the other hand, this methodological limit was in part balanced by a higher representativeness of the tested sample, as the waiting list only reflects the delay our department has between assessment and the first MBCT session, allowing us to recruit all patients. It is also important to note that in the observed therapeutic changes, a large number of factors could be involved (not all of them being tested herein), specific to MBCT or even shared across the various forms of psychosocial interventions. Finally, it was not possible to assess the total time devoted by patients to individual mindfulness practice in everyday life, although this parameter could have a significant impact on the efficacy of this therapy (Crane et al., 2014; Hawley et al., 2014; Perich et al., 2013).

Futher studies are needed to examine which are the core mecanisms involved in MBCT that can help reducing physiological reactivity, and to investigate if the reduction of SCR amplitude for negative emotions is in fact associated with improved emotion regulation and lower relapse rate following therapy.

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Table 1. *Sociodemographic and psychological characteristics at baseline, and SCR amplitude differences between baseline and pre-MBCT and between pre-MBCT and post-MBCT in Bipolar I patients*

Variables	Baseline (N=67)			Pre-MBCT (N=61)			Post-MBCT (N=61)			Baseline vs Pre-MBCT				Pre-MBCT vs Post-MBCT			
										t	Z	p	d	t	Z	p	d
Socioemographic and clinical characteristics	Mean	(SD)	%	Mean	(SD)	%	Mean	(SD)	%								
Age	47.69	10.55															
Gender (% females)			64.19%														
Age of onset	24.08	10.53															
Number of past depressive episodes	12.03	12.03															
Number of past (hypo)manic episodes	7.48	8.61															
Psychological characteristics																	
BDI-13	9.71	8.06		10.34	7.10		8.19	6.44		-1.291		0.202	0.083	**3.253**		**0.002**	0.317
DAS	140.97	33.92		144.30	35.01		129.43	35.34		-1.479		0.144	0.164	**4.539**		**0.001**	0.423
Subjective emotional responses – IAPS																	
Negative valence	1.96	0.78															
Neutral valence	5.13	0.85															
Positive valence	7.20	1.16															
Negative arousal	6.93	1.28															
Neutral arousal	2.20	0.83															
Positive arousal	6.70	1.38															
Patients with a significant change of the SCR response (%)																	
Positive pictures			25.4%			31.3%			34.3%								
Negative pictures			28.4%			35.8%			37.3%								
Neutral pictures			10.4%			11.9%			10.4%								
SCR amplitude (µSv)																	
Negative pictures	0.897	0.321		0.895	0.259		0.696	0.144		0.018		0.986	0.007	**2.219**		**0.042**	0.734
Positive pictures	0.783	0.213		0.887	0.315		0.735	0.189			-0.938	0.348	0.387		-1.779	0.075	0.519
Neutral pictures	0.518	0.132		0.557	0.132		0.528	0.127			-0.105	0.917	0.159		0.816	0.414	0.583

BDI-13 : Short version of the Beck Depression Inventory; DAS: Dysfunctional Attitudes Scale; IAPS: International Affective Picture System; SCR: skin conductance response. t for t-student test, Z for Wilcoxon non-paramteric test, d for effect size. Bold caracters reflates the presence of a significant difference

Figure 1. *SCR amplitude (in µSv) of bipolar I patients for positive, negative and neutral pictures, at baseline, pre-treatment and post-treatment*

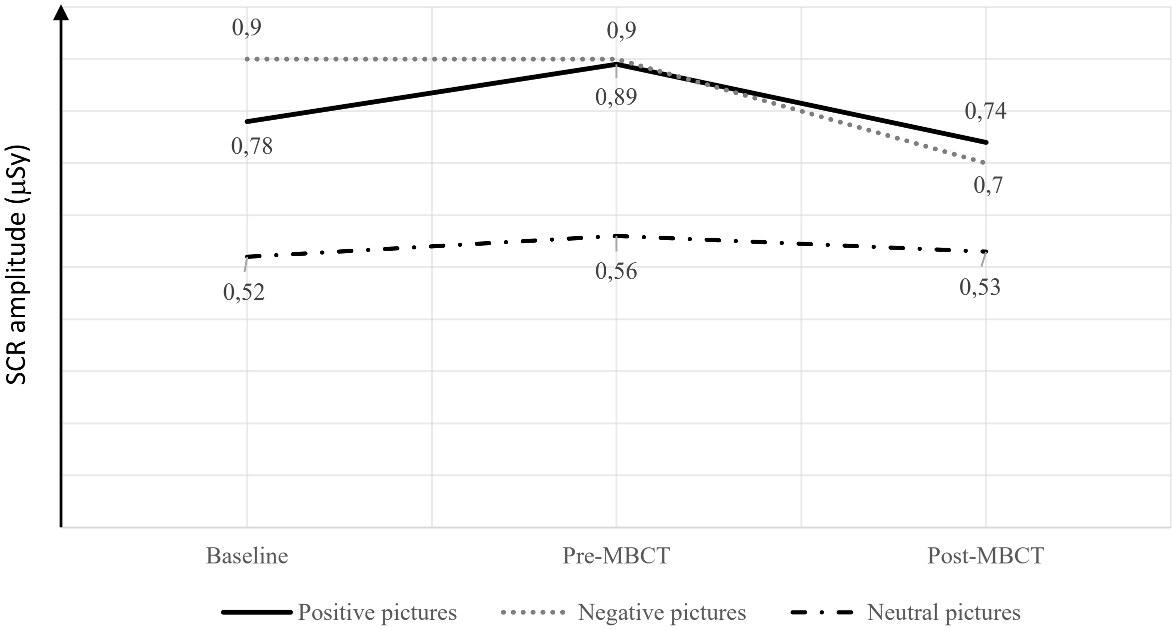

Figure 2. *Path-analysis comparing the direct effect of MBCT on the reduction of skin conductance amplitude when facing negative emotion stimuli, and a potential indirect effect through DAS improvement.*

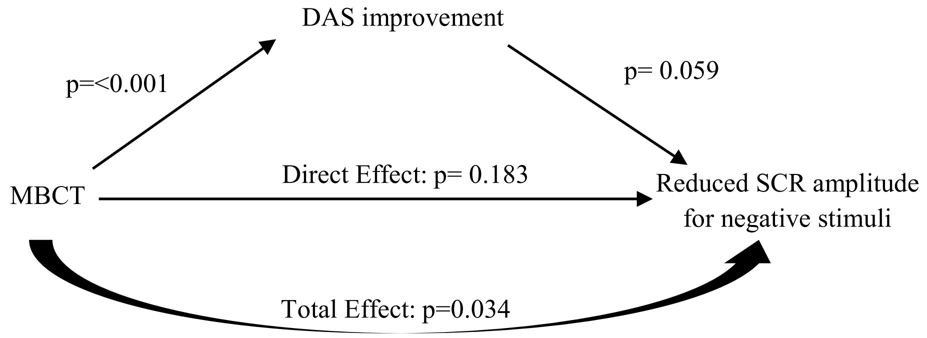

Table 2. *Predictive effect of dysfunctional attitudes at baseline on evolution of SCR amplitude to emotional pictures during MBCT for patients with Bipolar I disorder*

DV	IV	R^2	β	B	p	CI 95%	
						Min	Max
Evolution of SCR amplitude during MBCT							
Negative pictures	DAS scores at baseline	.340	.536	.007	**.039**	.000	.014
Positive pictures	DAS scores at baseline	.224	.426	.005	**.162**	-.002	.013
Neutral pictures	DAS scores at baseline	.011	.047	.000	**.948**	-.017	.018

DV = dependant variable; IV = independant variable; CI = confidence interval;

DAS: *Dysfunctional Attitudes Scale* ; SCR: *Skin conductance responses*